

REMARKS

With the amendment to the specification, the phrase regarding incorporation by reference has been deleted as required by the Examiner.

The amendments to Claims 1 and 9 find support in the specification, for example, at page 5, lines 5-8. No new matter is introduced by way of the amendments.

Applicants acknowledge the Examiner's withdrawal of the previous rejections under 35 U.S.C. §102(e) and 35 U.S.C. §103(a).

Claims 1, 4-9, and 12-16 are pending in the application, and Claims 1, 4-9, and 12-16 stand rejected. Claims 1, 4 and 7-8 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Blackburn, U.S. Patent No. 6,264,825 (hereafter "Blackburn"). Claim 5 stands rejected under 35 U.S.C. §103(a) as allegedly being obvious over Blackburn as applied to claim 1 and further in view of Roelant, U.S. Patent No. 6,001,573 (hereafter "Roelant"). Claim 6 stands rejected under 35 U.S.C. §103(a) as allegedly being obvious over Blackburn in view of Baselt, U.S. Patent No. 5,981,297 (hereafter "Baselt"). Claims 9, 12 and 15-16 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Blackburn in view of Brown et al., U.S. Patent No. 5,807,522 (hereafter "Brown"). Claim 13 stands rejected under 35 U.S.C. §103(a) as allegedly obvious over Blackburn in view of Brown as applied to Claim 9 and further in view of Roelant. Claim 14 stands rejected under 35 U.S.C. §103(a) as allegedly being obvious over Blackburn in view of Brown as applied to Claim 9 and further in view of Baselt. Claims 1, 4, 6-9, 12, and 14-16 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Baselt in view of Blackburn. Claims 5 and 13 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Baselt in view of Blackburn as applied to Claims 1 and 9 and further in view of Roelant.

Applicants respectfully traverse these rejections, and submit that the present claims are not obvious in view of the prior art. Applicants hereby incorporate by reference all previous arguments made in response to rejections in prior Office Actions in this and in the parent case, and in addition present the following arguments and remarks.

The Rejections of Claims 1, 4-9 and 12-16 Under 35 U.S.C. §103(a)

Claims 1, 4 and 7-8 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Blackburn.

In order to establish a prima facie case of obviousness, there must be: 1) some suggestion or motivation in the art or in the knowledge generally available to one of ordinary skill in the art, to modify or to combine the reference teachings; and 2) there must be a reasonable expectation of success; and 3) the prior art references must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on the applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Blackburn is presented by the Examiner as discussing a method for increasing the hybridization rate of nucleic acids in a sample comprising attaching probe nucleic acid molecules of known sequence to a solid support selected from the group consisting of silicon, glass and metals that is coated with a metal selected from silver, copper, gold, palladium and platinum, providing target nucleic acid molecules labeled with paramagnetic beads having a diameter of from about 1 nm (0.001 μ m) to about 200 μ m, attracting the labeled targets to the solid support by activating a magnetic field effective to induce rapid migration of the target, hybridizing the labeled target with their complementary pairs at a hybridization rate greater than the rate in the absence of the attracting field, washing the support and inverting the polarity of the magnetic field to remove unbound molecules and detecting the hybridized targets.

While Applicants do not agree with all aspects of the above interpretation of Blackburn, Applicants respectfully note that, even were such an interpretation of Blackburn to be correct, Blackburn would fail to make obvious the present invention.

As stated in *In re Paulsen* (30 F.3d 1475, 31 USPQ2d 1671 (Fed. Cir. 1994)) "the claimed invention must be considered as a whole." The claims of the present invention include many elements not discussed or suggested in Blackburn or other references. For example, Applicants note that the methods for increasing the hybridization rate of

nucleic acids in a nucleic acid assay of Claims 1, 4 and 7-8 all require at least the elements of providing probes attached to a solid support within multiple microwells, said microwells being at multiple locations on said support and being surrounded by coils suitable for producing localized DC magnetic fields, said microwells being connected by channels; and that the localized DC magnetic field produced by these coils within each of said microwells is effective to increase the rate of hybridization of the labeled nucleic acid target molecules with their complementary pairs within each of the microwells. In addition, the polarity of these DC magnetic fields within each of said microwells may be inverted to remove any unbound or nonspecifically bound molecules.

Blackburn fails to discuss or suggest such elements. Blackburn nowhere discusses or suggests coils for producing localized DC magnetic fields within microwells connected by channels. For example, although Blackburn does mention electrode coils (column 11, line 14), such electrode coils are not magnetic coils. As defined by Blackburn:

“By “electrode” herein is meant a composition, which, when connected to an electronic device, is able to sense a current or a potential and convert it to a signal. Alternatively an electrode can be defined as a composition which can apply a potential to and/or pass electrons to or from species in the solution.” (column 10, lines 54-59).

Thus, Blackburn fails to discuss or suggest coils suitable for producing localized DC magnetic fields and fails to discuss or suggest production of localized DC magnetic fields by such coils. Similarly, Blackburn fails to discuss or suggest localized DC magnetic fields within microwells, and fails to discuss or suggest inversion of localized DC magnetic fields within microwells.

Blackburn fails to discuss or suggest multiple microwells at multiple locations connected by channels. Blackburn also fails to discuss or suggest microwells surrounded by coils suitable for producing localized DC magnetic fields. In addition, Blackburn fails to discuss or suggest multiple microwells surrounded by coils at multiple locations, and fails to discuss or suggest connecting such microwells by channels.

Furthermore, failing to discuss or suggest at least these elements, Blackburn also fails to discuss or suggest, for example, a solid support having these elements, nor a solid support with such elements and being selected from the group consisting of silicon, glass, and metals that is or is coated with a metal selected from the group consisting of silver, copper, gold, platinum (II), mercury, mercury (II), thallium, cadmium (II), platinum (IV) and palladium (II).

Failing to discuss or suggest at least these elements, Blackburn also fails to discuss or suggest, for example, attracting labeled nucleic acid target molecules to such a solid support, nor attracting labeled nucleic acid target molecules to such a solid support by activating said coils to provide a localized DC magnetic field within each of said microwells effective to induce rapid migration of said labeled nucleic acid target molecules.

Furthermore, failing to discuss or suggest at least these elements, Blackburn also fails to discuss or suggest, for example, hybridizing the labeled nucleic acid target molecules with their complementary pairs at a hybridization rate greater than the hybridization rate in the absence of said attracting by said DC magnetic fields within each of said microwells.

Furthermore, failing to discuss or suggest at least these elements, Blackburn also fails to discuss or suggest, for example, washing the support and inverting the polarity of the DC magnetic fields within each of said microwells to remove any unbound or nonspecifically bound molecules. Applicants note that Blackburn, column 19, lines 29-65 does not discuss inverting the polarity of a magnetic field, and in particular does not discuss inverting the polarity of a localized DC magnetic field within a microwell.

Furthermore, failing to discuss or suggest at least these elements, Blackburn also fails to discuss or suggest, for example, detecting the hybridized target nucleic acid molecules attached to such a solid support.

Applicants respectfully note that the Examiner's description of Blackburn recites "labeling nucleic acid target molecules with paramagnetic beads having a diameter of

from about 1 nm (0.001 μm) to about 200 μm " (Office Action dated January 22, 2004, page 4, point 6, lines 8-9) and that Blackburn et al. "do not specifically teach the claimed diameter range of from about 1 nm to a10 nm." As discussed previously, such paramagnetic beads are typically much larger than the paramagnetic labels of the present invention. More importantly, Blackburn teaches that paramagnetic beads of the size cited by the Examiner are unsuitable for the purposes of the present invention:

"Microparticles of 4.5 μm have been observed to rest in solution on a solid support, relatively unaffected by diffusion, where as in the same sample 1.0 μm particles remain suspended away from the solid surface and appear to follow the constraints of diffusion." (column 22, lines 4-9).

Thus, Blackburn teaches that 1.0 μm paramagnetic particles are unsuitable for hybridization, since nucleotides attached to such small paramagnetic particles would not be in contact with a surface and so would be incapable of hybridizing. Thus, Blackburn refers to large particles, e.g., "beads" or "200 μm (magnetic particles)" when referring to shuttle particles which "associate with target analyte(s) in the assay solution" (column 19, lines 38-39) and not to paramagnetic labels having diameters of between about 1 nm to about 10 nm. Applicants respectfully submit that the paramagnetic labels of Claim 1, having a diameter of from about 1 nm to about 10 nm, are not properly characterized as "beads." Thus, Blackburn teaches away from the present invention, and does not render it obvious.

Applicants have discovered and disclosed that such small paramagnetic labels, e.g., those having a diameter of from about 1 nm to about 10 nm, are useful for attracting nucleic acid molecules to a solid support under the influence of a magnetic field in order to increase the hybridization rate with their complementary pairs. The present invention thus provides advantages over larger paramagnetic beads. Such advantages are unexpected in view of, for example, the teaching of Blackburn that such small paramagnetic labels would impede or prevent hybridization. The present disclosure teaches these advantages over the prior art, referring in part to beads, "the main problem with the use of these agents for hybridization of DNA is their size"

(page 5, lines 13-14). Thus, Applicants respectfully submit that Blackburn teaches away from, and does not make obvious, the paramagnetic label elements of the present invention.

Applicants respectfully note that the cited reference lacks at least the steps and elements discussed above, including, for example, providing target molecules consisting essentially of nucleic acid molecules labeled with paramagnetic labels having a diameter of from about 1 nanometer (nm) to about 10 nm attached to a solid support having coils suitable for producing localized DC magnetic fields within microwells connected by channels, and of attracting these labeled nucleic acid target molecules to such a solid support by activating a localized DC magnetic field within a microwell effective to induce rapid migration of the labeled nucleic acid target molecules, as required by some of the elements of the present invention.

Claims 4 and 7-8 include all the elements of Claim 1, and so also require at least all of the elements discussed above. In addition, these claims also require additional elements of, for example, the requirement that the paramagnetic labels comprise superparamagnetic particles (Claim 4), or that the nucleic acid molecules are oligonucleotides, genomic DNA, cDNA, RNA or fragments thereof (Claim 7), or that a probe or target is labeled with a fluorescent molecule (Claim 8).

In addition to failing to discuss all the elements of the claimed invention, Blackburn further provides no suggestion of these elements, and fails to provide motivation to supply the missing elements. Furthermore, in the absence of any suggestion of, or motivation to provide, the missing elements, Blackburn fails to provide any reasonable expectation of success for such a combination of elements. Lacking such disclosure of the missing elements, lacking suggestion or motivation to provide them, and failing to provide any reasonable expectation of success for such a combination, Applicants respectfully submit that the Blackburn does not make obvious Claims 1, 4 and 7-8. Accordingly, Applicants respectfully submit that the rejections to Claims 1, 4 and 7-8 under 35 U.S.C. §103(a) are overcome.

The Rejection of Claim 5 Under 35 U.S.C. §103(a)

Claim 5 stands rejected under 35 U.S.C. §103(a) as allegedly obvious over Blackburn as applied to claim 1 and further in view of Roelant.

Blackburn is described above, and in addition is described by the Examiner as discussing “washing the support and inverting the polarity of the magnetic field to remove unbound molecules and detecting the hybridized targets” (Column 6, lines 30-60; column 9, lines 31-61; column 21, lines 20-65; and column 38, line 61–Column 39, line 13), but is said by the Examiner to not describe “magnetic beads comprising porphyrins.” Roelant is presented by the Examiner as teaching a method similar to Blackburn, wherein “a porphyrin label provides a universal label which attaches irreversibly without bridging agents and can be detected in an amount which is proportional to the number of labeled particles.” The Examiner suggests that it would have been obvious to label the paramagnetic beads of Blackburn with the porphyrin label of Roelant. However, Applicants respectfully submit that Roelant does not teach or suggest the use of paramagnetic porphyrins to induce movement of particles in a localized DC magnetic field, and that Blackburn does not teach or suggest inverting the polarity of localized DC magnetic fields within multiple microwells surrounded by coils and connected by channels to remove any unbound or nonspecifically bound molecules.

In addition, Applicants respectfully note that the claims of the present invention nowhere recite “beads” and again respectfully note that the present disclosure teaches that beads are not suitable for the present invention: “the main problem with the use of these agents for hybridization of DNA is their size” (page 5, lines 13-14). Thus, Applicants respectfully submit that, at least this regard, the cited references do not apply to the present invention.

Moreover, Blackburn lacks many elements of the claimed invention, as discussed previously; Roelant does not provide such missing elements. For example, neither Blackburn nor Roelant discuss:

A solid support having multiple microwells at multiple locations, the microwells surrounded by coils suitable for producing localized DC magnetic fields within the microwells, the microwells being connected by channels;

providing probes attached to a solid support within such multiple microwells;

increasing the rate of hybridization of labeled nucleic acid target molecules with complementary pairs by activating a localized DC magnetic field within each of such microwells;

inverting the polarity of localized DC magnetic fields within multiple microwells connected by channels;

and other elements and actions.

Claim 5 depends from Claim 1. As discussed above, Blackburn and Roelant, even if combined, lack elements of Claim 1. Roelant does not supply these or other missing elements of the claimed invention. Claim 5 requires all the elements of Claim 1, and so requires elements not provided by the cited references. Moreover, the cited references provide no suggestion or motivation to provide the missing teachings. Lacking the missing teachings, and lacking any suggestion or motivation to provide them, the cited references also fail to provide any reasonable expectation of success of such a combination.

Accordingly, the cited references lacking at least these elements required to make the claimed invention obvious, providing no suggestion or motivation to be combined to provide the claimed invention, and failing to provide a reasonable expectation of success for such a combination, Applicants respectfully submit that the rejection of Claim 5 under 35 U.S.C. §103(a) is overcome.

The Rejection of Claim 6 Under 35 U.S.C. §103(a)

Claim 6 stands rejected under 35 U.S.C. §103(a) as allegedly being obvious over Blackburn in view of Baselt. Blackburn is presented by the Examiner as discussed above, and is further characterized by the Examiner as not specifically teaching cleavable conjugating attachment. Baselt is presented by the Examiner as providing a

method similar to that of Blackburn, in addition including a cleavable nucleic acid-bead attachment.

However, Baselt does not provide the elements discussed above that are lacking from Blackburn. For example, to list some but not all the elements lacking in Baselt, Baselt fails to provide a solid support having multiple microwells at multiple locations and connected by channels; microwells surrounded by coils suitable for producing localized DC magnetic fields within the microwells; probes attached to such a solid support; increasing hybridization rate by activating a localized DC magnetic field within each of such microwells; inverting the polarity of localized DC magnetic fields within multiple microwells connected by channels; and other elements.

Claim 6, which depends from Claim 1, requires all the elements of Claim 1, as well as the elements introduced in Claim 6 itself. Since Blackburn lacks at least the elements of Claim 1 discussed above, and since Baselt also lacks elements of Claim 1, the combination of Blackburn with Baselt also lacks at least these elements. Moreover, these references provide no suggestion or motivation to provide the missing teachings. Lacking the missing teachings, and lacking any suggestion or motivation to provide them, the cited references also fail to provide any reasonable expectation of success of such a combination.

Accordingly, the cited references lacking at least these elements of the claimed invention, Applicants respectfully submit that the rejection to Claim 6 under 35 U.S.C. § 103(a) is overcome.

The Rejections of Claims 9-12 and 15-16 Under 35 U.S.C. §103(a)

Claims 9, 12 and 15-16 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Blackburn in view of Brown.

Blackburn is presented by the Examiner as discussing a method for increasing the hybridization rate of nucleic acids in a sample comprising attaching probe nucleic acid molecules of known sequence to a solid support selected from the group consisting of silicon, glass and metals that is coated with a metal selected from silver, copper, gold, palladium and platinum, providing target nucleic acid molecules labeled with

paramagnetic beads having a diameter of from about 1 nm (0.001 μm) to about 200 μm , attracting the labeled targets to the solid support by activating a magnetic field effective to induce rapid migration of the target, hybridizing the labeled target with their complementary pairs at a hybridization rate greater than the rate in the absence of the attracting field, washing the support and inverting the polarity of the magnetic field to remove unbound molecules and detecting the hybridized targets, where the probe and target are both nucleic acids. The Examiner states that Blackburn does not specifically teach their method wherein the target is immobilized and the probe is labeled whereby a plurality of patient samples are simultaneously analyzed on the same solid support.

Brown is presented as providing a method wherein the target is immobilized and the probe is labeled.

While Applicants do not agree with all aspects of the Examiner's interpretation of Blackburn and of Brown, Applicants respectfully note that, even were such an interpretation of these references to be correct, the combination of Blackburn and Brown would fail to make obvious the present invention.

The claims of the present invention include many elements not discussed or suggested in Blackburn or in Brown. For example, Applicants note that the methods for increasing the hybridization rate of nucleic acids in a nucleic acid assay of Claims 9, 12 and 15-16 all require at least the elements of providing target molecules attached to a solid support within multiple microwells, said microwells being at multiple locations on said support and being surrounded by coils suitable for producing localized DC magnetic fields, said microwells being connected by channels; and that the localized DC magnetic field produced by these coils within each of said microwells is effective to increase the rate of hybridization of the labeled nucleic acid probe molecules with their complementary pairs within each of the microwells. In addition, the polarity of these DC magnetic fields within each of said microwells may be inverted to remove any unbound or nonspecifically bound molecules.

Both Blackburn and Brown fail to discuss or suggest such elements. Failing to discuss or suggest at least these elements, Blackburn and Brown also fail to provide

suggestion or motivation to combine with the other reference in order to provide the missing elements, even though, even if combined, many required elements would remain lacking. Failing to provide such motivation or suggestion to combine, and lacking required elements, Blackburn and Brown fail to provide one of ordinary skill in the art any reasonable expectation of success for such a combination.

Claims 12 and 15-16 require all the elements of Claim 9, and so also require at least all of the elements discussed above. In addition, these claims also require additional elements of, for example, the requirement that the paramagnetic labels comprise superparamagnetic particles (Claim 12), or that the nucleic acid molecules are oligonucleotides, genomic DNA, cDNA, RNA or fragments thereof (Claim 15), or that a probe or target is labeled with a fluorescent molecule (Claim 16). However, neither Blackburn nor Brown provide the missing elements discussed above, and so also fail to provide these elements further in combination with the additional elements required by Claims 12 and 15-16.

Accordingly, the cited references lacking at least these elements required to make the claimed invention obvious, Applicants respectfully submit that the rejections to Claims 9, 12 and 15-16 under 35 U.S.C. §103(a) are overcome.

The Rejection of Claim 13 Under 35 U.S.C. §103(a)

Claim 13 stands rejected under 35 U.S.C. §103(a) as allegedly obvious over Blackburn in view of Brown as applied to Claim 9 and further in view of Roelant.

Blackburn and Brown are presented by the Examiner as discussed above, the Examiner also stating that "they do not specifically teach the magnetic beads comprising porphyrins." Roelant is presented by the Examiner as providing a method similar to that of Blackburn and Brown, wherein the "porphyrin label provides a universal label which attaches irreversibly without bridging agents and can be detected in an amount which is proportional to the number of labeled particles." The Examiner suggests that it would have been obvious to label the paramagnetic beads of Blackburn with the porphyrin label of Roelant. However, as discussed above, Applicants respectfully submit that Roelant does not teach or suggest the use of paramagnetic

porphyrins to induce movement of particles in a localized DC magnetic field within microwells connected to other microwells by channels, among many elements of the claimed invention lacking from Roelant, and that Blackburn does not teach or suggest, for example, inverting the polarity of localized DC magnetic fields within multiple microwells surrounded by coils and connected by channels to remove any unbound or nonspecifically bound molecules.

In addition, Applicants again respectfully note that the claims of the present invention nowhere recite "beads" and that the present disclosure teaches that beads are not suitable for the present invention.

As discussed above, Blackburn and Roelant each also fail to teach or suggest many additional elements of the claimed invention. Failing to discuss or suggest such elements, Blackburn and Roelant also each fail to provide suggestion or motivation to combine with the other reference in order to provide the missing elements, even though, even if combined, many required elements would remain lacking. Failing to provide such motivation or suggestion to combine, and lacking required elements, Blackburn and Roelant fail to provide one of ordinary skill in the art any reasonable expectation of success for such a combination.

Accordingly, the cited references lacking at least these elements required to make the claimed invention obvious, Applicants respectfully submit that the rejection of Claim 13 under 35 U.S.C. § 103(a) is overcome.

The Rejection of Claim 14 Under 35 U.S.C. §103(a)

Claim 14 stands rejected under 35 U.S.C. §103(a) as allegedly being obvious over Blackburn in view of Brown as applied to Claim 9 and further in view of Baselt.

Blackburn et al. is presented by the Examiner as discussed above, and is described as lacking disclosure of a cleavable conjugating attachment. Baselt is presented by the Examiner as providing a method similar to that of Blackburn, wherein paramagnetic particles are attached to nucleic acid molecules using cleavable nucleic acid-bead attachment.

However, even if combined, the cited references fail to provide all the elements of Claim 14, which include all the elements of Claim 9 and further requires paramagnetic labels attached to the nucleic acid molecules using cleavable conjugating molecules. As discussed above, Blackburn, Brown and Baselt lack a number of the elements of Claim 9 and so also lack at least these elements of Claim 14, which depends from Claim 9.

Accordingly, the cited references lacking at least these elements required to make the claimed invention obvious, lacking suggestion or motivation to combine with the other references, failing even if combined to make Claim 14 obvious, and failing to provide any reasonable expectation of success if the references were to be so combined, Applicants respectfully submit that the rejection to Claim 14 under 35 U.S.C. § 103(a) is overcome.

The Rejections of Claims 1, 4, 6-9, 12, and 14-16 Under 35 U.S.C. §103(a)

Claims 1, 4, 6-9, 12, and 14-16 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Baselt in view of Blackburn.

Blackburn and Baselt are presented by the Examiner as discussed above. While applicants do not agree with all aspects of the Examiner's above interpretation of Baselt and of Blackburn, Applicants respectfully note that, even were such interpretations of these references be correct, the combination of Baselt and Blackburn would fail to make obvious the present invention.

For example, as discussed above, neither Baselt nor Blackburn provide a solid support having multiple microwells at multiple locations and connected by channels; microwells surrounded by coils suitable for producing localized DC magnetic fields within the microwells; probes attached to such a solid support within such multiple microwells; increasing hybridization rate by activating a localized DC magnetic field within each of such microwells; inverting the polarity of localized DC magnetic fields within multiple microwells connected by channels; and other elements.

Moreover, neither Baselt nor Blackburn provide any suggestion or motivation to provide the missing teachings. Lacking the missing teachings, and lacking any suggestion or motivation to provide them, the cited references also fail to provide any reasonable expectation of success of such a combination.

Accordingly, the cited references lacking at least these elements required to make the claimed invention obvious, Applicants respectfully submit that the rejections to Claims 1, 4, 6-9, 12, and 14-16 under 35 U.S.C. §103(a) are overcome.

The Rejections of Claims 5 and 13 Under 35 U.S.C. §103(a)

Claims 5 and 13 stand rejected under 35 U.S.C. §103(a) as allegedly obvious over Baselt in view of Blackburn as applied to claims 1 and 9 and further in view of Roelant.

As discussed above, Baselt and Blackburn fail to provide many of the elements required by Claims 5 and 13. Roelant similarly fails to provide at least the elements of a solid support having multiple microwells at multiple locations and connected by channels; microwells surrounded by coils suitable for producing localized DC magnetic fields within the microwells; probes attached to such a solid support within such multiple microwells; increasing hybridization rate by activating a localized DC magnetic field within each of such microwells; inverting the polarity of localized DC magnetic fields within multiple microwells connected by channels; and other elements. Thus, Roelant fails to make up for the disclosure lacking from Baselt and from Blackburn.

Roelant also fails to provide any suggestion or motivation to provide the missing teachings, which suggestion or motivation is also lacking from Baselt and from Blackburn. Lacking the missing teachings, and lacking any suggestion or motivation to provide them, the cited references also fail to provide any reasonable expectation of success of such a combination.

Accordingly, the cited references lacking at least these elements required to make the claimed invention obvious, Applicants respectfully submit that the rejections to Claims 5 and 13 under 35 U.S.C. §103(a) are overcome.

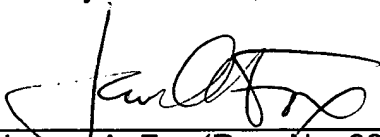
CONCLUSION

Applicants respectfully submit that all rejections and objections are overcome, and believe all claims to be in condition for allowance. Reconsideration and allowance of all pending claims is respectfully requested. Early notification of the allowance of the claims is respectfully requested.

The Commissioner is authorized to charge any fees, including any fees for extension of time, or credit overpayment to Deposit Account No. **08-1641** (Attorney's Docket No. **25527-0003 C1**).

Respectfully Submitted,

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